

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for generating proteins containing artificial SH3 domains having ligand binding affinity that is higher than the affinity of corresponding wild-type SH3 domain which comprises:

a) producing a collection of DNA fragments encoding SH3 domains containing a randomized mutations in a variable domain of an RT-loop (RRT-SH3 domains) that corresponds to amino acids 69-74 of Hck,

b) generating recombinant libraries comprising said variable RT-loop RRT-SH3 domains,

c) subjecting said libraries to affinity or functional selection steps to identify ~~artificial SH3~~ non-naturally occurring RT-loop domains, and

d) selecting proteins containing domains with an binding affinity that is higher than the binding affinity of the corresponding wild-type SH3 domain.

2. (Cancelled)

3. (Currently Amended) The method according to claim 1 ~~2~~, wherein the amino acid residues in the variable region of the RT-loop that are replaced comprise six amino acid residues that

immediately follow a conserved stretch of amino acids having an ALYDY (SEQ ID NO:1) consensus sequence.

4. (Previously Presented) The method according to claim 1, wherein the recombinant libraries comprise said RRT-SH3 domains in plasmid, phagemid or viral vectors.

5. (Withdrawn) An artificial SH3 domain, wherein amino acid residues in the variable region of its RT-loop have been replaced with any other amino acid residues.

6. (Withdrawn) The artificial SH3 domain according to claim 5, wherein said amino acid residues in the variable region of its RT-loop are the six amino acid residues corresponding to the residues 69 to 74 (EAIHHE) (SEQ ID NO:5) in the human Hck protein sequence.

7. (Withdrawn) An artificial SH3 domain derived from Hck-SH3 and targeted to the HIV-1 Nef protein, wherein the peptide motif EAIHHE (SEQ ID NO:5) in the variable region of its RT-loop has been replaced with a peptide motif selected from XSWSXX (SEQ ID NO:28, XSPFXX (SEQ ID NO:30) and XSXFPW (SEQ ID NO: 32), wherein X is any amino acid.

8. (Withdrawn) The artificial SH3 domain according to claim 7, wherein X is selected from V, F, D, M, P, S, T, W and Y (SEQ ID NOS:29 & 31).

9. (Withdrawn) The artificial SH3 domain according to claim 8, wherein the peptide motif is selected from VSWSPD (SEQ ID NO:6), FSWSDT (SEQ ID NO:7), DSWSTS (SEQ ID NO: 8), YSWSDM (SEQ ID NO:9), WSPFPS (SEQ ID NO:10), DSPFSF (SEQ ID NO:11), FSPFSF (SEQ ID NO:12), FSPFDW (SEQ ID NO:13), SSPFDW (SEQ ID NO:14), YSPFSW (SEQ ID NO:15), TSPFPW (SEQ ID NO:16), YS[P]FFPW (SEQ ID NO:17), YSDFPW (SEQ ID NO:18), and DSWFPW (SEQ ID NO:19).

10. (Withdrawn) An artificial SH3 domain derived from Hck-SH3 and targeted to the HIV-1 Nef protein, wherein the peptide motif EAIHHE (SEQ ID NO:5) in the variable region of its RT-loop has been replaced with a peptide motif selected from SSFYSS (SEQ ID NO:20), QGFLDQ (SEQ ID NO:21), NAFLPS (SEQ ID NO:22), EAWSPL (SEQ ID NO:23) and ESYSEW (SEQ ID NO:24).

11. (Withdrawn) A method for inhibiting, activating, or otherwise modifying the functions of cellular or pathogen-encoded proteins for research or therapeutic purposes, comprising expressing RRT-SH3 domains or derivatives thereof in cells comprising such proteins.

12. (Withdrawn) A diagnostic method for detecting an infectious organism, comprising detecting the binding of an RRT-SH3 domain or a derivative thereof to proteins of such an infectious organism.

13. (Withdrawn) A method for identifying novel protein targets for drug development, comprising expressing an RRT-SH3 domain or a derivative thereof in a cell to alter the behavior of said cell, and identifying an SH3-target protein involved in the altered function of said cell.

14. (Withdrawn) A method for identifying suitable molecular surfaces in known SH3 ligand proteins for guiding drug development, comprising using a RRT-SH3 domain or a derivative thereof to recognize the molecular region in its target protein that should be targeted by a drug in order to prevent similar interactions of this protein with naturally occurring SH3 domains.

15. (Withdrawn) A method for rational designing of drugs, comprising providing structural data of an RRT-SH3 domain or a derivative thereof, and designing drug candidates structurally mimicking said RRT-SH3 domain and sharing similar binding properties with said RRT-SH3 domain.

16. (Withdrawn) Method for identifying novel SH3 target proteins, comprising detecting the ability of proteins of interest to bind to an RRT-SH3 domain functionally selected as described in claim 1, or to a derivative thereof.

17. (Previously Presented) The method according to claim 3, wherein the six amino acids that are replaced in the RT-loop are replaced with a peptide motif derived from Hck-SH3 and which binds to HIV-1 Nef protein selected from the group consisting of XSWXXX (SEQ ID NO:28), XSPFXX (SEQ ID NO:30) and XSXFPW (SEQ ID NO:32), wherein X is any amino acid.

18. (Previously Presented) The method of claim 17, wherein X is an amino acid selected from the group consisting of V, F, D, M, P, S, T, W, and Y (SEQ ID NOS:29 and 30).

19. (Previously Presented) The method of claim 17, wherein the peptide motif is selected from the group consisting of VSWSPD (SEQ ID NO:6), FSWSDT (SEQ ID NO:7), DSWSTS (SEQ ID NO:8), YSWSDM (SEQ ID NO:9), WSPFPS (SEQ ID NO:10), DSPFSF (SEQ ID NO:11), FSPFSF (SEQ ID NO:12), FSPFDW (SEQ ID NO:13), SSPFDW (SEQ ID NO:14), YSPFSW (SEQ ID NO:15), TSPFPW (SEQ ID NO:16), YSFFPW (SEQ ID NO:17), YSDFPW (SEQ ID NO:18) and DSWFPW (SEQ ID NO:19).